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Statistical Distributions of Daily Breathing Rates for Narrow Age Groups of Infants and Children

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Children may be more susceptible to toxicity from some environmental chemicals than adults. This susceptibility may occur during narrow age periods (windows), which can last from days to years depending on the toxicant. Breathing rates specific to narrow age periods are useful to assess inhalation dose during suspected windows of susceptibility. Because existing breathing rates used in risk assessment are typically for broad age ranges or are based on data not representative of the population, we derived daily breathing rates for narrow age ranges of children designed to be more representative of the current U.S. children's population. These rates were derived using the metabolic conversion method of Layton (1993) and energy intake data adjusted to represent the U.S. population from a relatively recent dietary survey (CSFII 1994–1996, 1998). We calculated conversion factors more specific to children than those previously used. Both nonnormalized (L/day) and normalized (L/kg-day) breathing rates were derived and found comparable to rates derived using energy estimates that are accurate for the individuals sampled but not representative of the population. Estimates of breathing rate variability within a population can be used with stochastic techniques to characterize the range of risk in the population from inhalation exposures. For each age and age-gender group, we present the mean, standard error of the mean, percentiles (50th, 90th, and 95th), geometric mean, standard deviation, 95th percentile, and best-fit parametric models of the breathing rate distributions. The standard errors characterize uncertainty in the parameter estimate, while the percentiles describe the combined interindividual and intra-individual variability of the sampled population. These breathing rates can be used for risk assessment of subchronic and chronic inhalation exposures of narrow age groups of children.

KEY WORDS: Breathing rates; children; inhalation exposure; narrow age groups; statistical distributions

1. INTRODUCTION

There has been increased recognition that infants, prepubertal children, and adolescents (hereafter referred to collectively as children) may be more susceptible to the toxicity of some environmental chemicals than adults (Miller *et al*., 2002). Barton *et al*. (2005) analyzed animal data and found that early-life exposures may increase susceptibility to cancer. The U.S. EPA recently modified its risk assessment guidelines for mutagenic carcinogens from the traditional practice of considering all ages as having equal susceptibility to that of giving more weight to the 0 < 2 years (10× weight) and 2 < 16 years (3× weight) age groups. The revised approach is designed to account for the probable increased susceptibility to mutagenic carcinogens of these age groups relative to adults (U.S. EPA, 2005).

The period of greatest infant or child susceptibility to exposure to a particular chemical can last days,

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months, or years. This can be particularly important for young infants whose breathing rates, as well as biochemical and physiological parameters, change more rapidly than at any other time of life. Estimating dose and risk during susceptible periods is important in setting health standards, which are intended to protect the most susceptible members of the population. Breathing rates (volume of air inhaled per unit time) for narrow age periods are needed to best estimate inhalation dose during narrow periods of greatest susceptibility.

Beals *et al*. (1996) report a correlation between breathing rate (L/day) and body weight, which suggests that some of the variability in breathing rates is due to variability in body weight. Breathing rate variability is reduced by normalizing breathing rates to body weights (L/kg-day). Normalizing to body weight is also consistent with common risk assessment practices, where dose is expressed on a per body weight basis. Calculating the normalized rate for each individual allows for the assessment of interindividual variability of normalized rates.

Daily breathing rates are needed to estimate doses and risks from subchronic and chronic inhalation exposures. Ideally, daily breathing rates would be directly measured. However, the equipment for direct measurement is bulky and obtrusive and thus impractical for measuring breathing rates on children performing their typical activities over an entire 24-hour period. Two basic techniques have been developed to indirectly estimate daily breathing rates. One technique involves "coupling" minute breathing rates (directly measured) with daily time-activity pattern data (the number of minutes spent at each activity during 24 hours) (e.g., Marty *et al*., 2002). However, the coupling technique cannot provide accurate or representative breathing rates for the 0–6 year age group, or narrow age periods within this age group, because there is a paucity of minute breathing rate data for children 0–6 years of age. Existing breathing rate estimates developed using the coupling technique are limited because they apply to broad age ranges or were derived using minute breathing rate data only from children over six years of age.

The second technique for indirectly estimating daily breathing rates was proposed by Layton (1993). He reasoned that because the volume of oxygen needed to produce one kcal of energy was constant, and because the proportional volume of oxygen inhaled is constant, the amount of energy a person expends is directly proportional to the volume of air the person inhales. Layton (1993) developed an equation that models this relationship and that can be used to derive breathing rates from energy expenditure data:

$$\mathrm{VE} = H * \mathrm{VQ} * \mathrm{EE}.$$

In this equation, VE is the volume of air breathed per day (L/day), H is the volume of oxygen consumed to produce 1 kcal of energy (L/kcal), VQ (unitless) is the ratio of the volume of air to the volume of oxygen breathed per unit time and is referred to as the ventilation equivalent, and EE is energy (kcal) expended per day.

In his article, Layton presented daily breathing rates for children derived using two different sets of energy estimates. The first set was derived from food intake data from 1977–1978 (NFCS, 1977–1978), which is no longer the most current energy intake data available. The second set was estimated from data that were obtained using methods that are likely outdated (e.g., for the 0–3 years age group, 9 of the 11 studies were conducted between 1914 and 1952) and from select groups of children. Thus, the two sets of daily breathing rates presented by Layton are not representative of the full or current U.S. population of children, are not normalized to body weight, and for the second set, were for broad age ranges. Therefore, we chose to develop breathing rates for narrow age ranges of children using Layton's method with more recent and representative energy data than were available to Layton.

We sought energy data on each individual so that interindividual variability could be assessed and distributions of breathing rates could be derived. Breathing rate distributions can be used in stochastic risk assessment models to evaluate variability in risk from inhalation exposures. We also sought energy data paired with body weight for each individual so that breathing rates could be normalized to body weight for each individual.

One method that has been used to measure daily energy expenditure (EE) is the doubly labeled water (DLW) technique. This technique estimates average daily EE over a period of five to ten days and does not interfere with the performance of typical daily activities. However, the DLW method is expensive and requires the collection and analysis of daily urine samples, thus precluding its use in large-scale EE studies. Existing DLW studies were not designed to provide a statistically representative sample of the current U.S. population of children. The small sample sizes of DLW studies limit the robustness of statistical analyses, particularly the characterization of variability, which recently has been increasingly incorporated into risk assessment processes.

When individuals are weight stable (not gaining or losing weight), daily EE and daily energy intake (EI) (calories consumed) are equal. Even when individuals are gaining (or losing) weight over time, the fraction of daily EI that is used for weight gain (energy stored in tissues) is negligible relative to the vast majority of EE that is used for basal metabolism and physical activity (Layton, 1993). An exception is the weight gain of infants (see below). Thus, EI is a reasonable surrogate for EE in estimating breathing rates using Layton's method for noninfant children.

Several surveys have collected EI data representative of the U.S. children population. The most recent survey is the Continuing Survey of Food Intake for Individuals conducted from 1994 to 1996 and again in 1998 (hereafter referred to as CSFII); details can be found in USDA (2000). There are significant benefits to using the CSFII data set with Layton's method to derive daily breathing rates for risk assessments of children. Because daily EI and body weight (self-reported) are available for each individual, nonnormalized and normalized breathing rates for each individual can be derived. The age of each individual is also available so that rates can be accurately categorized into narrow age groups. CSFII-derived breathing rates better represent the current children's population than existing breathing rates because the CSFII is recent and included weighting factors designed to provide estimates representative of age and gender groups. Sample sizes for each age group were sufficiently large to provide statistical reliability for most analyses.

It is generally accepted that food intakes are often underreported or underestimated in dietary surveys for older children (Livingstone & Black, 2003). Layton (1993) calculated an underreporting adjustment factor of 1.2 and applied this value to data of children nine years of age and older for the EI-derived breathing rates in his article.

EI is used for basal metabolism, physical activity, and growth. EI used for growth has two components: (1) energy expended to synthesize macromolecules to be stored in tissue and (2) energy stored in these macromolecules. Since stored energy is not expended, and because Layton's method uses only expended energy, stored energy needs to be subtracted from EI when EI is used with Layton's method. However, the only period during childhood (and adulthood) when the energy put into storage is a significant proportion of EI is during early infancy, when 25–30% of EI is stored in new tissue (Butte *et al.*, 1989, 1995; Wells & Davies, 1998). Even during adolescent growth spurts, the energy needed for growth is not considered a significant proportion of energy intake (Spady, 1981; Butte *et al.*, 1989). Thus, to derive breathing rates for infants using Layton's method, the stored energy needs to be subtracted from EI. The study of Scrimshaw *et al*. (1996) provided the most useful estimates of stored energy with which to adjust EI. This is because both normalized and nonnormalized values were reported and because stored energy was estimated at relatively regular intervals through infancy. It should be noted that the Scrimshaw *et al.* values were for "energy of growth," which includes both energy to be stored and energy to synthesize macromolecules. However, energy for synthesis is a negligible proportion of EI (Butte *et al.*, 1989) and a small fraction of total energy for growth; therefore, energy of growth values are reasonable estimates of energy that is stored.

2. METHODOLOGY

The two-day-averaged daily EIs (kcal/day) of the CSFII data set were used with Layton's method to derive children's breathing rates. Children are defined as age 0–18 years (from birth up to but not including the 19th birthday), and include infants (0–11 months of age) and adolescents (9–18 years of age). Of the 11,147 records of children with two-day-averaged energy intakes, 572 (5%) did not report body weight and were excluded from our analyses. There were 502 children (4.5%) who reportedly consumed breast milk or were breastfed and were excluded from analyses of this article because energy intake from breast milk consumption was not measured and thus not included in CSFII estimates of EI. Though EI and body weight data were extensively reviewed for outliers, a systematic method to identify outliers was not found and potential outliers were not excluded.

To adjust for probable bias associated with underreporting of dietary intakes by older children, the EIs of children nine years of age and older were multiplied by 1.2, the value calculated by Layton (1993). The EI value (kcal/day) for each individual was divided by each individual's body weight (kg) to give normalized EI in kcal/kg-day. The Scrimshaw *et al.* combined-sexes mean energy of growth (energy put into storage) values were subtracted from the daily EI of the corresponding age infant in the CSFII to give energy-storage-adjusted daily EI for each infant.

The nonnormalized and normalized adjusted daily EIs were used in Layton's equation along with the conversion factors H and VQ, described below, to derive the final breathing rates for each individual. The resultant daily breathing rates were grouped into three-month age groups for infants, one-year age groups for children 1–18 years of age, and the age groups recommended by U.S. EPA to receive greater weighting for mutagenic carcinogens ($0 < 2$ and $2 < 16$ years) (U.S. EPA, 2005). It was hypothesized that there may be a difference in daily breathing rates between adolescent boys and girls based on differences in their minute breathing rates (Astrand, 1952; Rutenfranz *et al.*, 1981b). Therefore, daily breathing rates were derived for each gender of the age group 9–18 years.

2.1. H Values for Children

The amount of oxygen consumed ("H-nutrient") in metabolizing 1 gram of each type of energy-producing nutrient (carbohydrate, fat, and protein) has been measured in laboratories. Because a mix of these nutrient types are consumed by people each day, weighting each H-nutrient by its proportion in an average daily diet gives a total daily H. We calculated an H value of 0.22 from data of non-breastfed infants in the 1977–1978 NFCS and CSFII data sets and used this value to derive breathing rates for infants. An H value of 0.21 (Layton, 1993 and calculations of the 1977–1978 NFCS) was used for noninfant children.

2.2. VQ Values for Children

VQ is defined as the ratio of the volume of air to the volume of oxygen breathed per unit time. Layton (1993) presented a VQ value (27) calculated from adult data. Children have different respiratory minute ventilation rates, as well as other respiratory parameter values, relative to adults. Therefore, it was hypothesized that children's VQ values may differ from those of adults. A literature search and review were undertaken that sought studies reporting or containing data for calculating children's VQ values. Thirteen studies were identified that reported VQ data for children 4–18 years of age: Robinson (1938); Morse *et al.* (1949); Astrand (1952); Wilmore and Sigerseth (1967); Maksud *et al.* (1971); Rutenfranz *et al.* (1981a); Rutenfranz *et al.* (1981b); Rowland *et al.* (1987); Rowland and Green (1988); Inselman *et al.* (1993); Rowland and Cunningham (1997); Swaminathan *et al.* (1997); Guimaraes *et al.* (2001). The reported VQ values were weighted by sample size to derive a mean VQ value across studies. Separate preadolescent (4–8 years) and adolescent (9–18 years) VQ values were calculated because the literature suggests a difference in VQ values between preadolescent and adolescent children (Rowland & Green, 1988; Rowland & Cunningham, 1997). Separate VQ values were derived for adolescent boys and girls because they have different minute breathing rates (Astrand, 1952; Rutenfranz *et al.*, 1981b), which may contribute to differences in VQ. Because VQ data for children 1–3 years of age were not identified, the VQ value calculated for children 4–8 years of age (Table I) was used to derive the breathing rates for the one-, two-, and three-year-old age groups in this article. A distribution of VQ values was not evaluated because VQ values for individuals were not available.

Four studies were identified that provided VQ data for infants (Lagneaux *et al.*, 1988; Mortola *et al.*, 1992a, 1992b, 1995). Three of these four studies provided data on infants four days or less in age, a time period when breathing patterns are highly irregular. The fourth study (Lagneaux *et al.*) provided data on eight infants less than 20 days of age. This sample size is insufficient for reliable inference to the infant population and the infants' age cannot be considered representative of infancy (0–11 months). Therefore, the four studies were considered insufficient for deriving VQ values for infants. The VQ value calculated

Table I. Mean VQ Values Used to Derive Daily Breathing Rates

	Sample Size	Weighted Mean VQ	VQ Used for Present Article
Infants 0–11 months	na[1]	Insufficient or no data	33.5
Boys and girls 1–3 years	na[1]	Insufficient or no data	33.5
Boys and girls 4–8 years	217	33.5	33.5
Boys 9–18 years	587	30.6	30.6
Girls 9–18 years	598	31.5	31.5

[1] na = not applicable.

from data of children 4–8 years of age (VQ = 33.55) was used to derive breathing rates for the infant age groups presented in this article (Table I).

2.3. Statistical Analyses

The CSFII used a multistage complex sampling design to select individuals to be surveyed from the population. Sampling weights were calculated and then adjusted using postsurvey information and 17 selected demographic variables to allow for statistical results most representative of the population (Chu & Goldman, 1997; USDA, 2000). Jacknife Replication (JK) and Taylor Linearization are the primary statistical techniques used to analyze data from multistage complex surveys. For variance estimation (e.g., the SE), the JK and Taylor Linearization methods both incorporate information about the sampling design, but only the JK method results in unbiased variance estimates because it incorporates information about nonsampling weight adjustments (Flyer *et al.*, 1989; Wolter, 1985). The CSFII data set includes both sampling and JK replicate weights for each individual. We used a macro program developed by Gossett *et al.* (2002) that analyzes complex survey data using JK2, a specific type of JK. The Gossett *et al.* macro was run in version 8.2 of SAS (SAS Institute, 2002) to calculate the mean, SEM, percentiles, and SE of the 95th percentile using the CSFII-derived individual breathing rates (both nonnormalized and normalized), the sampling and replicate weights, and sampling design information (e.g., primary sampling unit). JK2 is a nonparametric technique.

Each age or age-gender data set was fit to the log-normal distribution using Crystal Ball® (Decisioneering, Inc., Denver, CO, 2000). For each age or age-gender group, 10,000 breathing rates were sampled using Latin-Hypercube sampling with probability of selection determined by the CSFII sampling weights. The weighted data were fit to the log-normal distribution and the geometric mean, *SD*, and 95th percentile were derived. The log-normal distribution is commonly used in stochastic risk assessment and has been found to be a reasonable parametric model for a wide variety of exposure parameters.

The same Latin-Hypercube analysis in Crystal Ball® was used to determine the best parametric model fit for the distribution of breathing rates for each age or age-gender group. Distributions were fit to each simulated data set and all continuous distributions were ranked for fit to the simulated data sets using Anderson-Darling statistics. The Anderson-Darling test was chosen over other goodness-of-fit tests available in Crystal Ball® (chi-square and Kolmorgorov-Smironov) because Anderson-Darling specifically gives greater weight to the tails than to the center of the distribution. We are especially interested in the tails since the right tail represents the highest breathing rates and thus potential high-end exposures in the population. The methods used for the log-normal, weibull, beta, gamma, and extreme value formulas are the polar marsaglia, inverse transformation, gamma density combination, rational fraction approximation with a Newton Polish step, and inverse transformation, respectively (Crystal Ball, 2000).

All estimated parameters in this article (means, SEMs, percentiles, SEs of 95th percentiles, geometric mean, *SD*s, 95th percentiles, and distributional parameter values) are estimates for the targeted populations (i.e., each age or age-gender group of the U.S. population) and not of the sample groups. Similarly, the distributional fits are intended to describe the targeted population and not the sample.

2.4. Comparisons to CSFII-Derived Breathing Rates

The CSFII-derived mean breathing rates were compared to the mean breathing rates estimated with DLW EE data that had been coupled with Layton's method and the conversion factors described in this article. The studies of Black *et al.* (1996), Torun *et al.* (1996), and Butte *et al.* (2000) were chosen to provide DLW EE data because together these studies covered the full spectrum of children's ages, included potentially more susceptible periods (i.e., early infancy, the first year of life, and adolescence), and represent a compilation of the majority of available DLW EE data. Because data on individuals from the DLW EE studies were not available, the mean values, and the age and age-gender groups defined in the DLW EE studies, were used to derive the comparison breathing rates. For consistency with the data used from the CSFII, only formula-fed, not breastfed, infant data from the Butte *et al.* study were used for comparison breathing rates. For consistency with age definitions in the CSFII, age was assumed to be the month (or year) following the specified age, unless otherwise specified.

3. RESULTS

The mean, SEM, 50th, 90th, and 95th percentiles, and SE of the 95th percentile of nonnormalized and

Table II. Nonnormalized Daily Breathing Rates (L/day) Derived Using Layton's Method, CSFII Energy Intake, and JK2 Methodology

Age	Sample Size (Nonweighted)	Mean	SEM	50%-ile	90%-ile	95%-ile	SE of 95%-ile
Age (months)			Infancy				
0–2	182	3,630	137	3,299	5,444[1]	7,104[1]	643
3–5	294	4,920	135	4,561	6,859	7,720	481
6–8	261	6,089	149	5,666	8,383	9,760	856
9–11	283	7,407	203	6,959	10,212	11,772	**
0–11 (infancy)	1,020	5,703	98	5,323	8,740	9,954	553
Age (years)			Children				
1	934	8,770	75	8,297	12,192	13,788	252
2	989	9,758	100	9,381	13,563	14,807	348
3	1,644	10,642	97	10,277	14,586	16,032	269
4	1,673	11,400	90	11,046	15,525	17,569	234
5	790	12,070	133	11,557	15,723	18,257	468
6	525	12,254	183	11,953	16,342	17,973	868
7	270	12,858	206	12,514	16,957	19,057	1,269
8	253	13,045	251	12,423	17,462	19,019	1,075
9	271	14,925	286	14,451	19,680	22,449[1]	1,345
10	234	15,373	354	15,186	20,873	22,898[1]	1,021
11	233	15,487	319	15,074	21,035	23,914[1]	1,615
12	170	17,586	541	17,112	25,070[1]	29,166[1]	1,613
13	194	15,873	436	14,915	22,811[1]	26,234[1]	1,106
14	193	17,871	615	15,896	25,748[1]	29,447[1]	4,382
15	185	18,551	553	17,913	28,110[1]	29,928[1]	1,787
16	201	18,340	536	17,370	27,555	31,012	2,065
17	159	17,984	957	15,904	31,421[1]	36,690[1]	**
18	135	18,591	778	17,339	28,800[1]	35,243[1]	4,244
Age (years)			Adolescent boys				
9–18	983	19,267	278	17,959	28,776	32,821	1388
Age (years)			Adolescent girls				
9–18	992	14,268	223	13,985	21,166	23,298	607
Age (years)	U.S. EPA Cancer Guidelines' Age Groups with Greater Weighting						
0 through 1	1,954	7,502	75	7,193	11,502	12,860	170
2 through 15	7,624	14,090	120	13,128	20,993	23,879	498

[1]FASEB/LSRO (1995) convention, adopted by CSFII, denotes a value that might be less statistically reliable than other estimates due to small cell size.
**Denotes unable to calculate.

normalized daily breathing rates, derived as described in this article, are presented in Tables II and III.

Overall, the CSFII-derived nonnormalized breathing rates (Table II) progressively increase with increasing age from infancy through 18 years of age while normalized breathing rates (Table III) progressively decrease. There were statistical differences between boys and girls 9–18 years of age, both for these years combined ($p < 0.00$) (Tables II and III), and for each year of age separately (not shown) ($p \leq 0.05$) (with the exception of the 10-year-old age group). Tables II and III also present breathing rates for the age groups recommended to receive greater weighting in risk assessments of mutagenic carcinogens in the U.S. EPA cancer guidelines supplement (2005). For both nonnormalized and normalized breathing rates, the 95th percentile was 1.5–1.9 times greater than the mean. In general, the 95th percentile SE was inversely proportional to sample size.

The geometric mean, *SD*, and 95th percentile of the log-normally fit distributions for each age and age-gender group are presented in Tables IV (nonnormalized breathing rates) and V (normalized breathing rates).

The best-fit distribution and corresponding distributional parameters for each age or age-gender group are presented in Tables VI and VII. The most frequent best fits among all age and age-gender groups for both nonnormalized and normalized rates were

Table III. Normalized Daily Breathing Rates (L/kg-day) Derived Using Layton's Method, CSFII Energy Intake, and JK2 Methodology

Age	Sample Size (Nonweighted)	Mean	SEM	50%-ile	90%-ile	95%-ile	SE of 95%-ile
Age (months)				Infancy			
0–2	182	839	42	725	1,305	1,614	290
3–5	294	709	24	669	1,031	1,232	170
6–8	261	727	16	684	1,017	1,136	73
9–11	283	760	20	710	1,137	1,283	96
0–11 (infancy)	1,020	751	11	694	1,122	1,304	36
Age (years)				Children			
1	934	752	7	716	1,077	1,210	33
2	989	698	9	670	986	1,107	31
3	1,644	680	6	648	966	1,082	18
4	1,673	645	5	614	904	1,011	19
5	790	602	7	587	823	922	25
6	525	550	10	535	765	849	28
7	270	508	9	495	682	788	39
8	253	458	11	439	657	727	37
9	271	466	11	445	673	766[1]	21
10	234	438	12	425	661	754[1]	38
11	233	378	9	350	566	616[1]	32
12	170	373	13	356	545[1]	588[1]	46
13	194	311	12	289	459[1]	588[1]	55
14	193	313	12	298	443[1]	572[1]	92
15	185	299	10	285	461[1]	524[1]	25
16	201	278	10	258	434	505	46
17	159	276	15	251	453[1]	538[1]	**
18	135	277	10	244	410[1]	451[1]	42
Age (years)				Adolescent boys			
9–18	983	367	5	343	567	647	14
Age (years)				Adolescent girls			
9–18	992	315	6	288	507	580	24
Age (years)	U.S. EPA Cancer guidelines' age groups with greater weighting						
0 through 1	1,954	752	6	706	1,094	1,241	24
2 through 15	7,624	481	3	451	764	869	6

[1]FASEB/LSRO (1995) convention, adopted by CSFII, denotes a value that might be less statistically reliable than other estimates due to small cell size.
**Denotes unable to calculate.

the gamma, extreme value, and log-normal distributions. Visually these three distributions are very similar as illustrated by the one-year olds' nonnormalized breathing rates in Fig. 1.

Tables VIII and IX list 95th percentiles calculated using the JK2 method, the modeled log-normal distributions, and the best-fit parametric model. The 95th percentiles differed between the three methods by 7% or less for all 114 calculated differences, and by 2% or less for 99 of the 114 differences (87%).

3.1. Comparison of Breathing Rates

Tables X, XI, XII, and XIII present comparisons of mean breathing rates derived using CSFII data with mean rates derived using DLW EE data. The CSFII and comparison rates are relatively similar.

4. DISCUSSION

Statistically significant differences were found in nonnormalized and normalized breathing rates between boys and girls 9–18 years of age. The fat-free mass (basically muscle mass) of boys typically increases during adolescence, associated with increased testosterone. Because fat-free mass is highly correlated to basal metabolism (Bitar *et al.*, 1999), and because basal metabolism accounts for the majority

Table IV. Parameter Estimates of Log-Normally Fit Distributions of Nonnormalized Breathing Rates (L/day)

Age/Age-Gender	Geometric Mean	Geometric *SD*	Sample Size (Nonweighted)	95th Percentile
Months 0–11 (infant)	5,242	1.55	1,020	9,957
Months 0–2	3,307	1.64	182	7,117
Months 3–5	4,684	1.37	294	7,791
Months 6–8	5,800	1.36	261	9,957
Months 9–11	7,039	1.38	283	11,874
1 year	8,357	1.37	934	13,830
2 years	9,320	1.36	989	14,824
3 years	10,223	1.33	1,644	16,394
4 years	10,943	1.34	1,674	17,604
5 years	11,602	1.33	790	18,260
6 years	11,788	1.32	525	18,280
7 years	12,446	1.29	270	19,095
8 years	12,590	1.31	253	19,371
9 years	11,952	1.32	271	22,562
10 years	12,232	1.37	234	22,909
11 years	12,368	1.37	233	23,993
12 years	13.756	1.43	170	29,352
13 years	12,477	1.40	194	26,532
14 years	13,834	1.45	193	29,659
15 years	14,264	1.50	185	30,616
16 years	14,009	1.58	201	31,146
17 years	13,267	1.64	159	38,321
18 years	14,177	1.52	135	36,097
Boys				
9–18 years	15,058	1.43	983	32,920
Girls				
9–18 years	11,491	1.41	992	23,551
U.S. EPA-weighted age groups				
0–1 year	6,885	1.55	1,954	14,122
2–15 years	13,189	1.43	7,624	23,835

of EE, nonnormalized breathing rates for adolescent boys may be expected to increase with increasing age. On average, adolescent girls do not achieve the same muscle mass as boys (20% less) so their basal metabolism and EE, and thus nonnormalized breathing rates, will be less than those of boys.

The best-fit distribution type for any given age or age-gender group was not influenced by sample or simulation size. For each age or age-gender group, the differences between the top three best-fit distributions (most frequently the log-normal, extreme value, and gamma) were marginally different, as supported by visual inspection. It may be concluded that all age and age-gender groups were best fit by skewed distributions with a right tail.

The 95th percentiles of the log-normal parametric model and best-fit parametric model differed from the JK2 95th percentiles by less than 7%. This indicates that the parametric models fit the right tails of the data fairly well.

The SE describes the uncertainty in the parameter estimate (e.g., the mean) by reflecting the dispersion of sample parameter estimates around the estimated population parameter. This uncertainty includes measurement and sampling errors, and biases for which we may not be able to account. Variability, on the other hand, characterizes the dispersion or distribution of breathing rate values within the population or within a person over time, and is described by the percentiles of the distribution.

The degree of applicability of daily measurements made over short periods (e.g., one to several days) to exposures that occur over months to years is unknown. Tests of agreement between the first and second day of CSFII energy intake measurements (3–10 days apart) are at high–moderate levels (0.58–0.78), suggesting that short-term intra-individual variability in the CSFII data is fairly small. Because neither energy intakes nor directly measured breathing rates over long periods of time (months to years)

Table V. Parameter Estimates of Log-Normally Fit Distributions of Normalized Breathing Rates (L/kg-day)

Age/Age-Gender	Geometric Mean	Geometric *SD*	Sample Size (Nonweighted)	95th Percentile
Months 0–11 (infant)	700	1.46	1,020	1,306
Months 0–2	740	1.69	182	1,710
Months 3–5	664	1.44	294	1,240
Months 6–8	692	1.37	261	1,137
Months 9–11	719	1.40	283	1,288
1 year	715	1.38	934	1,210
2 years	664	1.38	989	1,108
3 years	648	1.37	1,644	1,089
4 years	615	1.36	1,674	1,025
5 years	575	1.36	790	922
6 years	526	1.36	525	849
7 years	486	1.35	270	794
8 years	435	1.38	253	727
9 years	363	1.45	271	767
10 years	341	1.47	234	760
11 years	295	1.45	233	618
12 years	289	1.48	170	590
13 years	238	1.52	194	590
14 years	239	1.51	193	600
15 years	227	1.55	185	527
16 years	213	1.52	201	511
17 years	205	1.63	159	540
18 years	211	1.51	135	458
Boys				
9–18 years	280	1.53	983	647
Girls				
9–18 years	236	1.60	992	581
U.S. EPA-weighted age groups				
0–1 year	709	1.41	1,954	1,254
2–15 years	438	1.58	7,624	925

are available, long-term intra-individual variability in breathing rates cannot be assessed. The daily rates presented in this article were developed for risk assessments of subchronic or chronic (long-term) exposures. For less than daily exposure, one- or eight-hour rates are needed.

Although DLW EE data are considered highly accurate (Livingstone & Black, 2003), there are inherent differences between the adjusted CSFII EI and the DLW EE data used for our breathing rate comparisons, including differences in the sample or population represented and uncertainties in the measurement techniques. Thus, the DLW EE rates are not a gold standard for comparison but provide a useful gauge to judge approximate accuracy of the CSFII-derived breathing rates. The infants' CSFII-derived breathing rates were 15–27% greater than the comparison DLW EE breathing rates while the children's CSFII rates ranged from 23% less to 14% greater than comparison rates. Thus, despite methods, data, and some age definitions that differed between the comparison and CSFII-derived breathing rates, the CSFII and comparison rates are quite similar across age groups.

The VQ values used to derive breathing rates for this article were calculated from data extracted from available published studies. Though little is known about the variability of VQ, the extrapolation of VQ values from the 4–8 years age group to that of the 0–11 months and 1–3 years age groups is not likely to introduce significant error because the variability in VQ is likely to be small relative to variability from other factors that influence breathing rates. The VQ values presented in Table I are not derived from a representative sample of the children's population. Nonetheless, the derived VQ values are intended to be more applicable to infants and children than VQ values estimated from adult data. VQ measurements are made over short periods of time (minutes) and are influenced by the level of exercise (Astrand, 1952).

Table VI. Best-Fit Modeled Distributions and Parameters of CSFII-Derived Nonnormalized Daily Breathing Rates (L/day)

Age in Years	Distribution	Parameter Values	95%-ile
0–11 months	Extreme value	Mode = 4,645 scale = 1,891	9,967
1 year	Log-normal	Mean = 8780 *SD* = 2,826	13,830
2 years	Gamma	Location = 253 scale = 923 shape = 10	14,824
3 years	Gamma	Location = 1,057 scale = 960 shape = 10	15,888
4 years	Gamma	Location = 0 scale = 917 shape = 12	17,181
5 years	Gamma	Location = 0 scale = 942 shape = 13	18,260
6 years	Gamma	Location = 641 scale = 980 shape = 12	18,280
7 years	Log-normal	Mean = 12,856 *SD* = 3326	19,095
8 years	Gamma	Location = 1,297 scale = 1,029 shape = 11	19,371
9 years	Log-normal	Mean = 14,929 *SD* = 4,279	22,894
10 years	Logistic	Mean = 15,220 scale = 2,495	22,582
11 years	Log-normal	Mean = 15,489 *SD* = 4,613	23,699
12 years	Gamma	Location = 0 scale = 2,164 shape = 8	29,294
13 years	Log-normal	Mean = 15,849 *SD* = 5,572	26,686
14 years	Extreme value	Mode = 14,745 scale = 5,305	29,839
15 years	Weibull	Location = 4,035 scale = 16,392 shape = 2	31,066
16 years	Gamma	Location = 4,900 scale = 4,617 shape = 3	31,604
17 years	Log-normal	Mean = 18,070 *SD* = 9,678	38,885
18 years	Extreme value	Mode = 15,046 scale = 6,160	36,628
Boys			
9–18 years	Extreme value	Mode = 16,090 scale = 4,545	32,805
Girls			
9–18 years	Gamma	Location = 587 scale = 1747 shape = 8	23,552
U.S. EPA-weighted age groups			
0–1 year	Gamma	Location = 1,137, scale = 1,045, shape = 8	13,170
2–15 years	Extreme value	Mode = 11,719 scale = 4,055	25,626

Table VII. Best-Fit Modeled Distributions and Parameters of CSFII-Derived Normalized Daily Breathing Rates (L/kg-day)

Age	Distribution	Parameter Values	95%-ile
0–11 months	Extreme value	Mode = 623 scale = 223	1,306
1 year	Extreme value	Mode = 640 scale = 199	1,210
2 years	Gamma	Location = 97 scale = 83 shape = 7	1,108
3 years	Log-normal	Mean = 681 *SD* = 220	1,092
4 years	Gamma	Location = 55 scale = 67 shape = 9	1,003
5 years	Gamma	Location = 0 scale = 54 shape = 11	923
6 years	Gamma	Location = 41 scale = 54 shape = 9	849
7 years	Gamma	Location = 0 scale = 43 shape = 12	794
8 years	Extreme value	Mode = 390 scale = 120	727
9 years	Beta	Scale = 2726 alpha = 6.2 beta = 30	775
10 years	Gamma	Location = 0 scale = 59 shape = 7	749
11 years	Gamma	Location = 26 scale = 55 shape = 7	627
12 years	Weibull	Location = 87 scale = 323 shape = 2	590
13 years	Extreme value	Mode = 251 scale = 102	599
14 years	Extreme value	Mode = 254 scale = 100	609
15 years	Beta	Scale = 1205 alpha = 4.2 beta = 13	534
16 years	Gamma	Location = 63 scale = 76 shape = 3	511
17 years	Extreme value	Mode = 216 scale = 102	548
18 years	Gamma	Location = 26 scale = 52 shape = 5	452
Boys			
9–18 years	Extreme value	Mode = 297 scale = 122	647
Girls			
9–18 years	Gamma	Location = 40 scale = 77 shape = 4	581
U.S. EPA-weighted age groups			
0–1 year	Extreme value	Mode = 633 scale = 210	1,295
2–15 years	Gamma	Location = 1.77 scale = 97 shape = 5	880

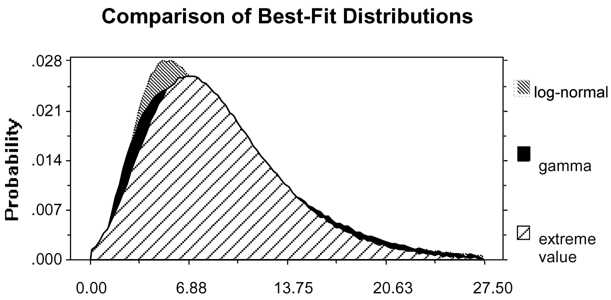

Fig. 1. Parametric distributional fits for nonnormalized one year of age breathing rates.

The VQ values presented in Table I were calculated from combining data of children at rest with data from children exercising at a submaximal energy expenditure level, to provide a daily VQ value that is likely relatively representative of the typical daily activity pattern of children. Thus, the VQ values presented in this article may be considered reasonable estimates of VQ for a 24-hour period based on the available data.

A potential source of bias in the CSFII is misreporting, underestimating, or overestimating of food intake. In addition to the underreporting of food intake by adolescents, there is also evidence that EI may be under- or overestimated for younger children (Fisher *et al.*, 2000) and that overweight children (or their parents) may underreport their food intakes (Maffeis *et al.*, 1994). It is possible that adolescents who misreport food intake may have misreported their body weights as well.

Though it is important to identify EI and body weight data points that may be outliers, available methods to identify such outliers have not been validated for skewed distributional types typical of many biological parameters, and outlier cutoff values are arbitrarily selected. Further, outlier detection methods such as the Goldberg cutoff (Livingstone & Black, 2003), which assesses the biological validity of self-reported EI, require certain data on each individual, which was not available in the CSFII data set.

The CSFII-derived breathing rates presented in this article compare well to breathing rates derived using other energy estimate data. The 95th percentiles of the CSFII-derived breathing rates are consistent when using different calculation methodologies. The CSFII-derived breathing rates may be considered reliable for use in the health risk assessment of subchronic and chronic inhalation exposures of infants and children, and especially useful for narrow age ranges, periods of suspected increased susceptibility, and for stochastic risk assessments.

Table VIII. Percentage Differences in 95th Percentiles of Nonnormalized Breathing Rates (L/day) Derived Using Different Methods

Age	95th Percentile JK2	95th Percentile Log-Normal	95th Percentile Best Fit	% Difference JK2 vs. Best Fit	% Difference JK2 vs. Log-Normal	% Difference Log-Normal vs. Best Fit
0–11 months	9,954	9,957	9,967	0.1	<0.1	0.1
1 year	13,788	13,830	13,830	0.3	0.3	0
2 years	14,807	14,824	14,824	0.1	0.1	0
3 years	16,032	16,394	15,888	0.9	2.0	3.7
4 years	17,569	17,604	17,181	2.3	0.2	2.4
5 years	18,257	18,260	18,260	0.0	<0.1	0
6 years	17,973	18,280	18,280	1.7	2.0	0
7 years	19,057	19,095	19,095	0.2	0.3	0
8 years	19,019	19,371	19,371	1.8	2.0	0
9 years	22,449*	22,562	22,894	1.9	0.5	1.5
10 years	22,898*	22,909	22,582	1.4	<.0.1	1.4
11 years	23,914*	23,993	23,699	0.9	0.3	1.2
12 years	29,166*	29,352	29,294	0.4	0.6	2.0
13 years	26,234*	26,532	26,686	1.7	1.0	0.6
14 years	29,447*	29,659	29,839	1.3	0.7	0.6
15 years	29,928*	30,616	31,066	3.7	2.2	1.8
16 years	31,012	31,146	31,604	1.9	0.4	1.4
17 years	36,690*	38,321	38,885	5.6	4.2	1.5
18 years	35,243*	36,097	36,628	3.8	2.4	1.4

Table IX. Percentage Differences in 95th Percentiles of Normalized Breathing Rates (L/kg-day) Derived Using Different Methods

Age	95th Percentile JK2	95th Percentile Log-Normal	95th Percentile Best Fit	% Difference JK2 vs. Log-Normal	% Difference JK2 vs. Best Fit	% Difference Log-Normal vs. Best Fit
0–11 months	1,304	1,306	1,306	0.1	5.6	0.1
1 year	1,210	1,210	1,210	0	0	0
2 years	1,107	1,108	1,108	<0.1	0.1	0
3 years	1,082	1,089	1,092	0.6	0.9	0.2
4 years	1,011	1,025	1,003	1.4	1.4	0.7
5 years	922	922	923	0	0.1	0.1
6 years	849	849	849	0	0	0
7 years	788	794	794	0.8	0.8	0
8 years	727	727	727	0	0	0
9 years	766*	767	775	0.1	1.2	1.0
10 years	754*	760	749	0.8	0.7	1.4
11 years	616*	618	627	0.3	1.8	1.4
12 years	588*	590	590	0.3	0.3	0
13 years	588*	590	599	0.3	1.8	1.5
14 years	572*	600	609	4.7	6.1	1.5
15 years	524*	527	534	0.6	1.9	1.3
16 years	505	511	511	1.1	1.2	0
17 years	538*	540	548	0.4	1.8	1.5
18 years	451*	458	452	1.5	0.2	1.3

Table X. Comparison of Mean Values of Infant Nonnormalized Daily Breathing Rates (L/day)

Age	Derived from Butte *et al.* (2000)	Derived from CSFII	% Difference
3 months	3296 ($N = 39$)	4341 ($N = 95$)	24%
6 months	4449 ($N = 37$)	5203 ($N = 83$)	14%
9 months	5373 ($N = 39$)	6541 ($N = 105$)	18%
12 months	5874 ($N = 39$)[1]	7581 ($N = 83$)[2]	23%

[1]At 12 months; [2]From the 11th month birthday up to the 12th month birthday.

Table XI. Comparison of Mean Values of Infant Normalized Daily Breathing Rates (L/kg-day)

Age	Butte *et al.* (2000) Derived Breathing Rate	CSFII-Derived Breathing Rates	% Difference
3 months	539 ($N = 39$)	688 ($N = 95$)	22%
6 months	574 ($N = 37$)	674 ($N = 83$)	11%
9 months	605 ($N = 39$)	692 ($N = 105$)	13%
12 months	597 ($N = 39$)[1]	755 ($N = 83$)[2]	21%

[1]At 12 months; [2]From the 11th month birthday up to the 12th month birthday.

Table XII. Comparison of Mean Values of Children's Nonnormalized Daily Breathing Rates (L/day)

Age (Years)	Gender	Comparison Breathing Rate	Sample Size	CSFII-Derived Breathing Rate	CSFII Sample Size	Percentage Difference[1]
Compare to Black *et al*. (1996)						
1–6	Both	10,316	50	10,734	6,555	4%
7–12	Boys	16,274	32	15,439	740	−5%
7–12	Girls	13,535	24	13,843	691	2%
13–17	Boys	22,686	31	20,668	467	−9%
13–17	Girls	18,875	26	14,524	465	−23%
Compare to Torun *et al*. (1996)						
7–8	Both	13,824	35	12,948	523	−6%
9–16	Boys	17,556	47	18,349	837	5%
9–16	Girls	15,015	57	14,710	844	−2%

[1]Negative sign indicates that the CSFII rate is less than the comparison rate.

Table XIII. Comparison of Mean Values of Children's Normalized Daily Breathing Rates (L/kg-day)

Age (Years)	Gender	Comparison Breathing Rate	Sample Size	CSFII Breathing Rate	CSFII Sample Size	Percentage Difference[1]
Black *et al*. (1996)[1]						
2–3	Both	622	23	687	2,633	9%
3–4	Both	587	58	662	3,317	11%
4–5	Both	544	34	631	2,463	14%
5–6	Both	550	58	581	1,315	5%
6–7	Both	533	23	536	795	<1%
Torun *et al*. (1996)[1]						
7–8	Both	529	35	484	523	−9%
9–16	Boys	394	47	387	837	−2%
9–16	Girls	340	57	341	844	<1%

[1]Negative sign indicates that the CSFII rate is less than the comparison rate.

REFERENCES

Astrand, P. O. (1952). *Experimental Studies of Physical Working Capacity in Relation to Sex and Age*. Copenhagen: Munksgaard.

Barton, H. A., Cogliano, V. J., Flowers, L., Valcovic, L., Woodrow Setzer, R., & Woodruff, T. J. (2005). Assessing susceptibility from early-life exposure to carcinogens. *Environmental Health Perspectives*, *113*, 1125–1133.

Beals, J. A., Funk, L. M., Fountain, R., & Sedman, R. (1996). Quantifying the distribution of inhalation exposure in human populations: Distribution of minute volumes in adults and children. *Environmental Health Perspectives*, *104*(9), 974–979.

Bitar, A., Fellmann, N., Vernet, J., Coudert, J., & Vermorel, M. (1999). Variations and determinants of energy expenditure as measured by whole-body calorimetry during puberty and adolescence. *American Journal of Clinical Nutrition*, *69*, 1209–1216.

Black, A. E., Coward, W. A., Cole, T. J., & Prentice, A. M. (1996). Human energy expenditure in affluent societies: An analysis of 574 doubly-labelled water measurements. *European Journal of Clinical Nutrition*, *50*, 72–85.

Butte, N. F., Moon, J. K., Wong, W. W., Hopkinson, J. M., & Smith, E. O. (1995). Energy requirements from infancy to adulthood. *American Journal of Clinical Nutrition*, *62*(Suppl), 1047S–1052S.

Butte, N. F., Wong, W. W., & Garza, C. (1989). Energy cost of growth during infancy. *Proceedings of the Nutrition Society*, *40*, 303–312.

Butte, N. F., Wong, W. W., Hopkinson, J. M., Heinz, C. J., Mehta, N. R., & Smith, E. O. (2000). Energy requirements derived from total energy expenditure and energy deposition during the first 2 y of life. *American Journal of Clinical Nutrition*, *72*(6), 1558–1569.

Chu, A., & Goldman, J. D. (1997). Sample design. In K. S. Tipett & Y. S. Cypel (Eds.), *Design and Operation: The Continuing Survey of Food Intake by Individuals and the Diet and Health Knowledge Survey, 1994–96*. U.S. Department of Agriculture, Agricultural Research Service, NFS Report No. 96-1.

FASEB/LSRO (Federation of American Societies for Experimental Biology, Life Sciences Research Office). (1995). Joint policy on variance estimation and statistical standards on NHANES III and CSFII reports (Appendix III). In *Third Report on Nutrition Monitoring in the United States. Prepared for the Interagency Board for Nutrition Monitoring and Related Research*. Washington, DC: U.S. Government Printing Office

Fisher, J. O., Johnson, R. K., Lindquist, C., Birch, L. L., & Goran, M. I. (2000). Influence of body composition on the accuracy of reported EI in children. *Obesity Research*, *8*(8), 597–603.

Flyer, P., Rust, K., & Morgenstein, D. (1989). Complex survey variance estimation and contingency table analysis using replication. Proceedings of the Survey Research Methods Section, American Statistical Association, January 4–6, 1989, San Diego, CA. Available at http://www.amstat.org/sections/srms/proceedings/papers/1989_017.pdf.

Gossett, J. M., Simpson, P., Parker, J. G., & Simon, W. L. (2002). How complex can complex survey analysis be with SAS®? [abstract]. Proceedings, SAS Users Group International Meeting, Orlandao, April 14-17, 2002 (Cary, NC: SAS Institute Inc.). Paper 266–27.

Guimaraes, G. V., Bellotti, G., Mocelin, A. O., Camargo, P. R., & Bocchi, E. A. (2001). Cardiopulmonary exercise testing in children with heart failure secondary to idiopathic dilated cardiomyopathy. *Chest*, *120*(3), 816–824.

Inselman, L. S., Milanese, A., & Deurloo, A. (1993). Effect of obesity on pulmonary function in children. *Pediatric Pulmonology*, *16*, 130–137.

Lagneaux, D., Mossay, C., Geubelle, F., & Christiaens, G. (1988). Alveolar data in healthy, awake neonates during spontaneous breathing: A preliminary investigation. *Pediatric Pulmonology*, *5*(4), 225–231.

Layton, D. W. (1993). Metabolically consistent breathing rates for use in dose assessments. *Health Physics*, *64*(1), 23–36.

Livingstone, M. B., & Black, A. E. (2003). Markers of the validity of reported energy intake. *Journal of Nutrition*, *133*, 895S–920S.

Maffeis, C., Schultz, Y., Zaffanello, M., Piccoli, R., & Pinelli, L. (1994). Elevated energy expenditure and reduced energy intake in obese prepubertal children: Paradox of poor dietary reliability in obesity? *Journal of Pediatrics*, *124*(3), 348–354.

Maksud, M. G., Coutts, K. D., & Hamilton, L. H. (1971). Oxygen uptake, ventilation, and heart rate. *Archives of Environmental Health*, *23*(1), 23–28.

Marty, M. A., Blaisdell, R. J., Broadwin, R., Hill, M., Shimer, D., & Jenkins, M. (2002). Distribution of daily breathing rates for use in California's Air Toxics Hot Spots Program risk assessments. *Human and Ecological Risk Assessment*, *8*(7), 1723–1737.

Miller, M. D., Marty, M. A., Arcus, A., Brown, J., Morry, D., & Sandy, M. (2002). Differences between children and adults: Implications for risk assessment at California EPA. *International Journal of Toxicology*, *21*(5), 403–418.

Morse, M., Schultz, F. W., & Cassels, D. E. (1949). Relation of age to physiological responses of older boy (10–17 years) to exercise. *Journal of Applied Physiology*, *1*, 683–709.

Mortola, J. P., Frappell, P. B., Dotta, A., Matsuoka, T., Fox, G., Weeks, S., & Mayer, D. (1992a). Ventilatory and metabolic responses to acute hyperoxia in newborns. *American Review of Respiratory Disease*, *146*, 11–15.

Mortola, J. P., Frappell, P. B., Frappell, D. E., Vellena-Cabrera, N., Vellena-Cabrera, M., & Pena, F. (1992b). Ventilation and gaseous metabolism in infants born at high altitude, and their responses to hyperoxia. *American Review of Respiratory Disease*, *148*, 1206–1209.

Mortola, J. P., Saiki, C., & Fox, G. (1995). Insusceptibility of the Hering-Breuer reflex to spontaneous changes in metabolic rate in the infant. *Clinical Science (Colch)*, *89*(1), 101–105.

Robinson, S. (1938). Experimental studies of physical fitness in relation to age. *Arbeitephysiologie*, *10*, 251–323.

Rowland, T. W., Auchinachie, J. A., Keenan, T. J., & Green, G. M. (1987). Physiologic responses to treadmill running in adult and prepubertal males. *International Journal of Sports Medicine*, *8*, 292–297.

Rowland, T. W., & Cunningham, L. N. (1997). Development of ventilatory responses to exercise in normal white children. *Chest*, *111*, 327–332.

Rowland, T. W., & Green, G. M. (1988). Physiological responses to treadmill exercise in females: Adult-child differences. *Medicine and Science in Sports and Exercise*, *20*(5), 474–478.

Rutenfranz, J., Andersen, K. L., Seliger, V., Klimmer, F., Berndt, I., & Ruppel, M. (1981a). Maximum aerobic power and body composition during the puberty growth period: Similarities and differences between children of two European countries. *European Journal of Pediatrics*, *136*(2), 123–133.

Rutenfranz, J., Andersen, K. L., Seliger, V., Klimmer, F., Ilmarinen, J., Ruppel, M., & Kylian, H. (1981b). Exercise breathing during the growth spurt period: Comparison between two European countries. *European Journal of Pediatrics*, *136*(2), 135–142.

Scrimshaw, N. S., Waterlow, J. C., & Schurch, B. (Eds.). (1996). *Energy and Protein Requirements*. Proceedings of an International Dietary and Energy Consultancy Group Workshop; 1994 Oct 31–Nov 4; London, UK: Stockton Press.

Spady, D. W. (1981). Determination and expression of energy requirements. Joint FAO/WHO/UNU Expert Consultation on Energy and Protein Requirements: EPR 81 4; 1981 Oct 5–17; Rome, Italy. FAO Corporate Repository M2760/E; 2002. Available at http://www.fao.org/DOCREP/MEETING/004/M2760E/M2760E00.htm.

Swaminathan, S., Vijayan, V. K., Venkatesan, P., & Kuppurao, K. V. (1997). Aerobic capacity and cardiopulmonary response to exercise in healthy South Indian children. *Indian Pediatrics*, *34*, 112–118.

Torun, B., Davies, P. S., Livingstone, M. B., Paolisso, M., Sackett, R., & Spurr, G. B. (1996). Energy requirements and dietary energy recommendations for children and adolescents 1 to 18 years old. *European Journal of Clinical Nutrition*, *50*(Suppl 1), S37–S80; discussion S80–81.

Wells, J. C. K., & Davies, P. S. W. (1998). Estimation of the cost of physical activity in infancy. *Archives of Disease in Childhood*, *78*, 131–136.

Wilmore, J. H., & Sigerseth, P. O. (1967). Physical work capacity of young girls 7–13 years of age. *Journal of Applied Physiology*, *22*, 923–928.

Wolter, K. M. (1985). *Introduction to Variance Estimation*. New York: Springer-Verlag.

U.S. Department of Agriculture (USDA), Agricultural Research Service. (2000). *Continuing Survey of Food Intake by Individuals (CSFII) 1994-96, 1998*. CD-ROM.

U.S. Environmental Protection Agency (EPA). (2005). *Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens, Risk Assessment Forum*. (EPA/630/R-03/003F). Washington, DC.